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REMARKS

Claims 1-19 are pending. Claims 1-14 are as originally filed in the present application and claims 15-19 have been added in the current response.

No new matter has been added. Specifically, support for newly added claims is present on pages 3-7 of the specification as well as in originally-filed claims 1-4 and 11.

A. Restriction Requirement/ Species Election

Applicants elect Group I without prejudice to pursuing the originally presented or cancelled subject matter in a later application claiming benefit of this application, and particularly without prejudice to determination of equivalents of subject matter of this application or any later application claiming benefit of this application.

The Examiner has also required a species election when Group I has been elected by the Applicants. In compliance with this requirement, Applicants select a species defined by Formula I, wherein B is α -amino-butyric acid, U is (D)-alanine, X is absent, and Y is (2'-Br)Ph. Claims 1-4, and 11 read on the elected species.

B. Specification/Claim Objections

Applicants have amended the abstract to be clear and concise and in a narrative form not exceeding 150 words.

Applicants have amended the specification to include the terms "nuclear factor of activated" T cells, "human immunodeficiency virus", "chronic obstructive pulmonary disease", "human cytomegalovirus", "heat shock protein" 70, "dimethylsulfoxide", "mitogen-activated protein kinase", "Chinese hamster ovary" cells, "albino brown agouti" mice, and "[4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid]," which are well known in the art as definitions corresponding to the acronyms "NFA", "HIV", "COPD", "HCMV", "HSP70", "DMSO", "MAP" kinase, "CHO" cells, "CBA" mice, and "HEPES" respectively at their first instance of recitation in the specification. Applicants point out that the acronym "PMA", as used in the specification, stands for "protein kinase C activator phorbol ester" and is spelled out in its first

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instance at page 31, line 29. On page 32, line 27 of the specification, "OFL, female mice" has been amended to correct a typographical error which now reads "CF1, female mice."

Applicants also point out that the acronym "HBSS", as used in the specification, stands for "Hank's balanced salt solution", and is spelled out in its first instance of use at page 34, lines 9-10 in the specification.

C. Rejections Under 35 U.S.C. § 102(b)

Claims 1-4 and 11 have been rejected as being anticipated by Bollinger *et al.*, EP 0296122. It is stated in the action that:

Bollinger et al disclose a cyclosporin structure that meets the limitation of the Formula (I) structure of claim 1 of the instant application (see page 5 formula (II) wherein "B" is α Abu, "X" is Sar, "Y" is Val, and "A" is set forth in formula (XIX) on page 19, wherein " R_6 " group has the meaning given in formula (V) (see the second line, page 20), wherein formula (V) describes that " R_6 " group is phenyl). Note that the reference patent is applied to "A2" moiety. Because Applicant elects "B" as α -amino butyric acid, "U" as -(D) alanine, "X" as absent, and "Y" as (2'-Br)Ph for patent examination, and because Bollinger's patent also teaches that the phenyl group is further subject to Halogen substitution (see lines 35-37, page 8), claims 2-4 are anticipated by the reference as well. (Action, page 6).

Applicants disagree. For a generic chemical formula of compounds to anticipate a claimed species covered by the formula, the species must be "at once envisaged" from the formula. See MPEP § 2131.02. Stated differently, "anticipation can only be found if the classes of substituents are sufficiently limited or well delineated (emphasis added)." See MPEP § 2131.02 (citing *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990)).

Applicants submit that the elected species of the instant application cannot be "at once envisaged" by one of ordinary skill in the art. In the Bollinger reference, " R_6 " of formula (V) is "hydrocarbyl" which is further defined as "includ[ing] aromatic, aliphatic and araliphatic groups, whereby aliphatic groups and moieties may be branched or straight chain" (Bollinger at page 8, line 34). Hydrocarbyl aromatic groups are known in the art to include any cyclic hydrocarbon moiety having $4n+2 \pi$ electrons. Examples of hydrocarbyl aromatic groups

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which are known in the art include, but are not limited to, naphthyl, azulenyl, anthracenyl, phenyl, and the like. In addition, hydrocarbyl aliphatic groups can be comprised of any number of carbon atoms in straight chain or branched form having any degree of unsaturation. Examples of hydrocarbyl aliphatics include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, tert-butyl, pentyl, neopentyl, hexyl, heptyl, octyl, vinyl, butenyl, pent-3-enyl, and the like. Hydrocarbyl araliphatics are known in the art as any hydrocarbyl aromatic moiety linked via a hydrocarbyl aliphatic group as previously discussed. Hydrocarbyl araliphatic groups would include, but not be limited to, 3-naphthylpropyl, 3-naphthyl-2-methyl-propyl, 6-azulenylhexyl, styrene, phenethyl, and the like. Applicants submit that the terms defining "hydrocarbyl" in the Bollinger reference encompass hundreds, if not thousands, of possible cyclosporin derivatives. Accordingly, Applicants submit that because of the expansive language employed to define "hydrocarbyl" and the enormous plurality of possible compounds that fall within formula (V) of the Bollinger reference, the elected species cannot be "at once envisaged" by one of ordinary skill in the art. Thus, in accordance with M.P.E.P. § 2131.02, the Bollinger reference cannot operate as an anticipation of the Applicant's elected species.

Applicants further point out that, although the only substitution described for the R₆ group is halogen or hydroxy (Bollinger page 8, line 36), these substitutions can be at any one of a large number of positions present on any one of the possible R₆ hydrocarbyl groups. One of ordinary skill in the art, therefore would not "at once envisage" Applicant's elected species among the vast plurality of groups encompassed by Bollinger's definition of hydrocarbyl and the enormous number of possible halogen or hydroxy-substituted hydrocarbyl groups. Applicants accordingly submit that the Bollinger reference is not sufficient to constitute an anticipatory reference within the scope of M.P.E.P. § 2131.02.

Applicants still further submit that the preferred hydrocarbyl groups for R₆ of formula (V) describe only unsubstituted groups as being preferred (Bollinger page 8, lines 37-41). The recitation of the most preferred groups for R₆ are "phenyl and C₁₋₅alkyl" does not describe preferred substitution on either of these groups, thus inferring unsubstitution as being preferred. (Bollinger page 8, lines 40-41). The Bollinger reference, in reciting specific

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preferred species, fails to describe even one halogen substituted phenyl for R₆. The only disclosed halogen-substituted species in the Bollinger reference is a non-aryl species bearing a bromide (Bollinger page 8, line 60). The expressed teachings provided by the Bollinger reference preferred species, therefore, will not lead one of ordinary skill in the art to the Applicant's elected species. Applicants thus submit that the Bollinger reference is not sufficient to constitute an anticipatory reference within the scope of M.P.E.P. § 2131.02.

In view of the preceding remarks, Applicants respectfully request that the claim rejections be reconsidered and withdrawn in the instant application.

Applicants submit that newly added claims 15-19 are also not anticipated by the Bollinger reference as applied by the Examiner.

D. Provisional Rejections-Obviousness Type Double Patenting

Claims 1-4 and 9 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 and 9 of copending Application No. 09/975923 and claims 1-3 and 8 of Application No. 09/9800856. (Action page 7).

Applicants disagree with the assertions in the Action regarding obvious structural variation. Applicants will address these issues upon maturation of any of the instant or cited applications into a granted patent.